

Aus der ehem. II. Chirurgischen Abteilung des Bürgerspitals Basel

(Chefarzt: Prof. Dr. H. Heusser)

(Arbeit unter Leitung von PD Dr. G. Rutishauser)

Hypernephroma

An Analysis of 113 Cases from Three Continents

Inaugural-Dissertation

zur Erlangung der Doktorwürde der gesamten Heilkunde
der Medizinischen Fakultät der Universität Basel

vorgelegt von

Eric Bienstock

von New York / USA

Basel 1965

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Dedicated to
Sandy and Laurie

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Introduction

The *purpose of this paper* is to contrast the relevant clinical, diagnostic, therapeutic and prognostic findings of hypernephroma patients in the New York Metropolitan area with hypernephroma cases treated in two other continents. Thirty patients treated in the following New York hospitals serve as the basis for this paper (*Table I*):

Table I. New York Hospitals participating in the study

1958-1963	surgical patients	hypernephromas
Meadowbrook Hospital	28,219	12
New Rochelle Hospital	21,761	11
Grasslands Hospital	5,398	4
Knickerbocker Hospital	10,316	3
	65,694	30

Forty-seven patients treated during the same period at the II. Chirurgische Abteilung des Bürgerspitals Basel, Switzerland and analyzed by *Bienstock* and *Laufer*, serve as a comparison. The results attained by *Laufer*¹¹ in his thirty-six cases at Tel Hashomer Hospital of Tel-Aviv, Israel (1958-1963) are also contrasted. Additional relevant references are included.

Hypernephroma (renal cell carcinoma, Grawitz tumor, hypernephroid tumor) constitutes about 85 % of the malignant renal neoplasms. These tumors are characterized by a destructive growth with a marked tendency for early vessel-invasion and distant metastasis. The etiology is unknown.

The name "hypernephroma" stems from the old concept that this neoplasm arises from adrenal cortical inclusions in the kidney. The present view is that it originates from cells of the renal tubule epithelium or from renal adenomas.

Hypernephroma is an infrequent tumor: *Balogh and Szendrői*² found 196 cases in seventeen years at the Budapest medical school; *Lenkei*¹² 42 cases in twenty years at the Kantonsspital (University Hospital) of Zürich; and *Beer*⁴ 25 cases at the II. Chirurgische Abteilung des Bürgerspitals Basel from 1950-1956. *Ljunggren*¹⁵ had 58 cases in twenty years in a Stockholm hospital. Our own studies confirm these literature findings, as is evident in *Table II*.

Table II. Frequency of hypernephromas per 1000 surgical patients (1958-1963)

	Total surgical patients	Total hypernephroma patients	hypernephroma cases per 1000 surgical patients
New York	65,834	30	0,3
Basel	41,537 *)	47	1,1
Tel-Aviv	20,184	36	1,7

The low incidence found in the New York study is explained by the fact, that the Basel and Tel-Aviv patients were treated in urology departments or surgical departments with urology, while the New York patients were treated in general surgical hospitals.

Incidence

In the literature a 2:1 = *male:female ratio* is most commonly found (^{3, 12, 20}). Our New York cases (67 % females) reveal a 1:2 = *male:female ratio*. The same relationship is found if we examine the six Negro patients in the group. In contrast, however, Basel with 62 % males and Tel-Aviv with 58 % males show a predominance of males over females. Out of the total of 113 patients in three studies, 52 % were males and 48 % females; a very slight difference.

Age

The peak incidence of hypernephroma is said to occur during the sixth decade of life and the greatest concentration of cases are found in the fifth, sixth and seventh decades (^{1, 3, 12, 20}). As evident in *Table III* the New York, Basel and Tel-Aviv results concur with the literature finding.

Table III. Age distribution of hypernephroma

Years	New York	Basel	Tel-Aviv
30-50	23 %	7 %	31 %
51-70	50 %	58 %	69 %
71-90	27 %	35 %	-

It is interesting to note that almost 31 % of the Tel-Aviv cases occurred before the age of 51 and that no cases were found after 71 years of age. It is likely that the immigrants to Israel did not adjust very easily to the local conditions and climate, and thus a lowered life expectancy resulted.

History

The past history and family history of hypernephroma patients are generally found to be negative (^{2, 3}). In the New York study two patients had kidney stones several years before the tumor developed. Nephrolithiasis was also found in the majority of the 16 Tel-Aviv cases with pre-

*) Patients of the Chirurgischen Universitätsklinik and the II. Chirurgischen Abteilung des Bürgerspitals Basel.

vious kidney disease. It is well known that Israel has a high rate of nephropithiasis possibly because of its dry climate. In the Basel group two patients had kidney stones while two others had histories of pyelitis. In the light of these facts it does not seem likely that preexisting kidney disease has an important causal role in hypernephroma.

2. Symptomatology

In order to present a clear picture of the importance of various symptoms found in hypernephroma, it was decided to discuss them under the following subtitles:

- non specific tumor symptoms in hypernephroma
- specific symptoms of hypernephroma
- special pathophysiological signs in hypernephroma which as yet have not been fully explained.

The frequency of *non-specific tumor symptoms* in hypernephroma is presented in *Table IV*.

Table IV. Non-specific tumor symptoms in hypernephroma

Symptom	New York	Basel	Tel-Aviv
weight loss	16 %	32 %	36 %
anemia	37 %	55 %	25 %
elevated sedimentation rate . . .	75 %	82 %	53 %

Weight loss does not seem to be a very early symptom in hypernephroma. Although a severe loss in a short period of time was noticed in five New York patients, only two presented with weight loss as their first symptom. In Basel, out of 15 patients who had lost weight during the course of the disease, only two showed this loss as a first symptom. Approximately the same relation held true for the Tel-Aviv patients.

On the basis of normal values for hemoglobin of 11–16 gm % for females and 13–16 gm % for males, 37 % of the patients in the New York study showed *anemia* at the time of the diagnosis. The lowest hemoglobin value was 4.5 gm % in a female patient. Basel with 55 % and Tel-Aviv with 25 % had both higher and lower values respectively. In the literature we find an average of 40 % (¹³, ¹⁹) which corresponds to our findings. It is evident that anemia in the later course of hypernephroma occurs quite frequently and can be severe.

Basel with 82 % and Tel-Aviv with 53 % of *elevated sedimentation rate* concur with the high rate recorded in various works (¹³, ¹⁹). Out of four sedimentation tests done in the New York group three were abnormally high (75 %). This important screening test for malignancy was neglected in the majority of the New York cases, possibly because of financial reasons. *Voute*²³ found the sedimentation rate generally neglected in the American literature.

Among the *specific symptoms* of hypernephroma, *hematuria*, *tumor*, and *pain* are often described as the "classical diagnostic triad". In addition, acute varicocoele is mentioned as being a rather specific symptom. Table V presents a comparison of these symptoms as found in the three surveys:

Table V. *Specific symptoms of hypernephroma*

	Hematuria	Tumor	Pain	Varicocoele
New York	60 %	40 %	23,3 %	3 %
Basel	70 %	16 %	42,5 %	16 %
Tel-Aviv	75 %	47 %	64 %	—

The table shows decisively that *hematuria* is by far the most important symptom.

Generally three reasons are given for the bleeding: renal pelvis invasion by the extremely well vascularized tumor gives rise to macrohematuria and is certainly a more important source than the bleeding ascribed by some authors (^{2, 3}), to either tumor-induced venous compression or toxic blood vessel damage. In the literature hematuria is found to occur in 25–90 % of the cases (^{1, 2, 15, 20}).

As a first symptom, hematuria occurred in 56,6 % of the New York cases. Unfortunately hematuria as a first symptom does not mean that it is also an early symptom since the tumor is usually located well within the parenchym and the bleeding occurs first upon renal pelvis invasion. Together with the Basel and Tel-Aviv groups hematuria as a first symptom was found in 58 % of all the patients.

Tumor as a first sign seems to be infrequent. According to various sources (^{12, 15, 23}) a figure close to 10 % represents the maximum number of cases with a palpable mass of the costovertebral angle as the first sign. In the New York study there were two patients (6,6 %) who presented with costovertebral angle enlargement as their first symptom. However, once admitted to the hospital, the total number of palpable masses rose to 13, presumably because a costovertebral angle mass was specifically sought. A similar picture was observed in the Basel and Tel-Aviv groups in which 0,4 % and 5,5 % of the patients respectively showed a palpable mass as their first symptom. It is difficult to palpate the kidney in an adult. In an obese person and in those patients in which the tumor is located at the upper pole this difficulty will increase. Thus, unless the mass is extremely large it will seldom present as the first symptom. Kidney palpation, therefore, does not seem to be a very satisfactory method of screening patients for hypernephroma.

In order to cause *pain* the tumor has to be large. The pain may be caused by increased tension of the capsule due to the renal tumor, pressure on neighboring organs, or through necrotic tissue in the ureter, which may cause a colic. In the literature pain is generally considered a late symptom (^{2, 6, 15, 23}). Pain as a first symptom was experienced by 23 % of the New York patients. Three of them had continuous costovertebral angle pain while in the other four cases the pain was localized in the

abdomen and low back. The incidence of patients who had pain as their first symptom was 43 % in Basel and 64 % in Tel-Aviv. These findings emphasize the fact that, although not an early symptom, pain as a first symptom was present in a large number of our patients and therefore, seems to be a more important diagnostic indicator in hypernephroma than is generally accepted.

A *symptomatic varicocoele* is occasionally given as a sign of renal tumors (2, 10, 16, 18). External pressure on the Vena spermatica or invasion of the renal vein causes increased hydrostatic pressure in the plexus pampiniformis and leads to venectasis. In men acute right sided varicocoele should probably be of greater diagnostic importance, than a left sided one. A left sided varicocoele can occur for hemodynamic reasons even without a kidney tumor.

In the literature the percentages given vary greatly: *Lenkei*¹² found varicocoele in 22 % of the tumor cases while *Ljunggren*¹⁵ found only 3 %. The rather small number found in New York: 3 %; Basel: 16 %; and Tel-Aviv: 0 %, seem to confirm that a varicocoele has only minor diagnostic value. A varicocoele was found infrequently in the New York and Tel-Aviv patients while 16 % were diagnosed in Basel and 50 % in Zürich¹², possibly indicating a more meticulous search for this symptom in the Swiss hospitals.

Table VI presents three signs which although found in many other diseases, have a certain significance in hypernephroma. Their cause is still obscure but sometimes they can be of a definite value in the diagnosis of the disease.

Table VI. Special pathophysiological signs in hypernephroma which as yet have not been explained.

Sign	New York	Basel	Tel-Aviv
fever	42 %	11 %	50 %
polycythemia	7 %	6 %	3 %
hypertension	37 %	21 %	14 %

The cause of fever in hypernephroma is not fully known. The theories which are discussed include:

- pyrogenic material released by tumor cell destruction acts as a stimulant for the thermoregulatory center
- allergic reaction caused by tumor proteins
- large scale tumor necrobiosis.

If we consider oral temperature of 37,4° as the upper limit of normal, then 42 % of the New York patients had fever in the preoperative course of their disease. Of these, nine had a continuous low grade fever, while only one patient had "characteristic" fever spikes. As a first symptom fever was not found in any of the New York patients. In the Basel group 1,6 % of the patients had fever as an early symptom, while the Tel-Aviv study shows 15,8 %. In the literature the values range from 7 % - 40 % (2, 3, 12, 23).

In regard to the pathophysiology of fever, it is interesting to note that in the New York study only six out of ten patients with fever had metastasis. *Bottiger*⁶ found even fewer febrile cases in patients with metastasis. Thus it seems unlikely that metastasis is primary cause of fever.

Lately the question of *polycythemia* is much discussed in connection with renal pathology (^{13, 21, 22}). Hemoglobin values of over 16 gm % and red blood cell counts of over 5 million were considered to be indicative of this condition. Polycythemia occurring with hypernephroma may be due to increased blood plasma levels of an erythropoietic stimulating factor, which is formed by tumorous kidney tissue. Up to the present, 52 cases of polycythemia in hypernephroma have been observed²³. In the New York study there were two polycythemia cases while one case was found in the Tel-Aviv material and three in the Basel group. Thus polycythemia although neither a frequent nor an early sign, has nevertheless been more frequently diagnosed in the past few years.

Hypertension is not a very frequent finding in hypernephroma. In the literature the values given range from 9–25 % (^{10, 13}). Several theories as to the origin of tumor-induced hypertension are advanced:

- partial renal vascular compression or obstruction (*Goldblatt* phenomenon)
- endocrine function of the tumor.

*Minder*¹⁶ justly claims that the blood pressure in kidney tumors is generally not raised. If the blood pressure is elevated, one has to consider primarily other etiologies for hypertension. A preoperative blood pressure increase of over 140/90 was found in 37 % of the New York cases and 21 % and 14 % of the Basel and Tel-Aviv groups respectively. In the three studies systematic pre- and postnephrectomy readings were not done and it is therefore very difficult to draw a definite conclusion concerning the frequency and origin of the hypertension.

As a first sign, elevated blood pressure was found in 2,7 % of the Tel-Aviv patients, 0,2 % of the Basel cases, and 0 % of the New York patients. It seems, as with polycythemia, hypertension in hypernephroma is an infrequent and an unreliable sign and is therefore of no major diagnostic importance.

3. Diagnosis

The methods used to ascertain the diagnosis and their respective values are presented in *Table VII*.

Table VII. Methods used to ascertain the diagnosis of hypernephroma

Method	New York	Basel	Tel-Aviv
clinical examination	10 %	—	57 %
pyelography	73,3 %	82 %	74,5 %
angiography	—	17,8 %	8,6 %
retroperitoneal air insufflation .	3,3 %	—	2,8 %
exploratory lumbotomy	13,3 %	8,9 %	2,8 %

Diagnosis by *clinical examination alone* was made in only five (4,5 %) of the 113 cases. No tumors were diagnosed by this manner in Basel.

Intravenous Pyelography may not be conclusively diagnostic early in the disease and in advanced cases the concentration of the contrasting medium in the diseased pelvis may be poor. At all times this method is of great value in screening and determining the function of the other kidney, but for definite diagnosis *retrograde pyelography* is often needed. In the New York group 73,3 % were diagnosed through pyelography, in Basel and Tel-Aviv the figures are only slightly different: 82 % and 74,5 % respectively. These high percentages show the overwhelming diagnostic importance of this radiologic procedure. Without any doubt the early diagnosis of hypernephroma rests almost entirely upon it.

Nephroangiography is always indicated when pyelography fails to clarify the condition. This method was not yet used in the New York hospitals during the period of our study. In Basel 17,8 % of the cases had to be confirmed by angiography, while in Tel-Aviv 8,6 % were so ascertained.

Retroperitoneal air insufflation has lost much of its diagnostic value since the popularization of nephroangiography. It was used only once in New York and once in the Basel group. *Balogh and Szendrői*² claim that the method should not be used anymore because it may cause serious complications.

Exploratory lumbotomy was resorted to when all other methods failed to diagnose the condition. The obvious advantage of this procedure is that it affords direct palpation and offers the possibility of immediate histologic diagnosis. It seems characteristic that a relatively high number of the New York cases (13,3 %) in which nephroangiography was not used, were diagnosed by exploratory lumbotomy while Basel and Tel-Aviv with 8,9 % and 2,8 % respectively show a lower percentage.

Cytologic examination of the urinary sediment which is sometimes proposed for early diagnosis of tumors of the urinary tract does not offer the possibility of an early diagnosis of hypernephroma. This is due to the fact that this parenchymal tumor has no primary contact with the renal pelvis. However, if hematuria has already occurred, the method could be an important diagnostic tool. In the New York group six out of seven patients tested in this way showed negative results. This underlines the fact that cytology of the urinary sediment is only conclusive if positive but by no means does a negative result exclude a tumor. We agree with the opinion of *Balogh and Szendrői*² and *Voute*²³ who state that the test is therefore of limited use.

4. Metastasis

Although hypernephroma is well known for its ability to metastasize to almost any organ in the body, the sites listed in *Table VIII* were affected most often:

Table VIII. Kidney veins invasion and the most frequent sites of metastasis

Site *)	New York	Basel	Tel-Aviv
Kidney veins invasion	44 %	54 %	78 %
Bones	44 %	50 %	10 %
Lung	28,5 %	65 %	33 %
Peri-renal capsule	2,5 %	32 %	52 %
Regional lymph nodes	15 %	24,6 %	13 %

It was confirmed at operation and through autopsy that 70 % of the New York patients had metastasis out of which 33 % were already present on hospital admission. The Basel cases with 43 % metastasis show a considerably lower percentage than that of the Tel-Aviv cases (66 %). In the literature, metastasis at the time of the diagnosis ranges from 17 %–41 % (12, 23). The reason that the patients in Basel had less metastasis than in the other two groups, is possibly because in Basel the time from the discovery of the first symptom to operation was generally shorter.

According to Robbins¹⁸ 10–15 % of hypernephroma cases which came to autopsy had metastasis in the other kidney. The New York and Tel-Aviv studies revealed on autopsy 4,7 % and 6,6 % kidney metastasis while 0 % was found in the Basel group. Beckmann³ in his series had 4,7 %. Hypernephroma metastasis to the contralateral kidney therefore seem to be rather uncommon.

5. Therapy

Nephrectomy is the treatment of choice when the patient's condition and the local invasion of the tumor are considered. The frequency of operative therapy is shown in Table IX.

Table IX. Frequency of operative therapy

Treatment	New York	Basel	Tel-Aviv
operation	73 %	92 %	64 %
conservative treatment	27 %	8 %	36 %

Preoperative radiation in order to provide better conditions for the operation as proposed by Bally and Love¹ was not done in any of the three groups.

Postoperative radiation was used in 20 % of the New York cases and in 39 % and 70 % of the Tel-Aviv and Basel cases respectively. It is generally believed that hypernephroma is radioresistant. Since cytostatica have been used only once in the Tel-Aviv and New York studies and three times in the Basel group one may justly conclude that presently these drugs are unreliable in the treatment of hypernephroma. Radiation therefore, is the only therapeutic means remaining to prevent tumor recurrence and to treat cases with inoperable metastasis. However, in our study, the

*) Based on autopsy and biopsy material.

prognosis of the radiated patients does not differ markedly from that of the non-radiated patients.

Nephrectomy in hypernephroma is often not very easy considering the topographic situation of the kidney, the possibility of a short renal pedicle and a big infiltrating tumor with venous congestion. It is clear that no single incision will meet all requirements. The *operative methode* used are listed in *Table X*.

Table X. Operative methods used

Operation method	New York	Basel	Tel-Aviv
lumbo-retroperitoneal	77 %	81 %	100 %
abdominal trans-peritoneal . . .	23 %	5 %	—
thoraco-abdominal	—	14 %	—

Although the thoraco-abdominal access has definite advantage in cases with large tumors, the usual method used is still the lumbo-retroperitoneal approach. Possibly the thoraco-abdominal method is not used very frequently because it is feared that it might adversely affect the immediate postoperative prognosis in view of the extensive nature of the operation. The successful thoraco-abdominal operations in Basel however disprove this claim.

No operation mortality is reported in any of the three studies.

6. Prognosis

Since the cases examined were taken from the 1958–1963 period, the five year survival rate can not be evaluated. The material in *Table XI* has been gathered in a different manner in order to reflect a possible prognostic difference in the therapy used.

Table XI. Prognosis of hypernephroma patients with and without postoperative radiation

	New York	Basel	Tel-Aviv
nephrectomy without radiation			
died within one year.	19 %	20 %	45 %
alive until October 1963	81 %	81 %	55 %
nephrectomy with postoperative radiation			
died within one year.	63 %	21 %	28 %
alive until October 1963	37 %	79 %	72 %

The factors which might have helped to determine this prognosis are reviewed in the discussion.

7. Discussion

The purpose of this work was to contrast the clinical findings of hypernephroma patients treated during the same time interval in three

different continents. The influence of geography, different population cross sections, methods of treatment etc. were to be reviewed in order to compare the clinical course and prognosis of the disease. Although no surprising results emerge from this study and the figures obtained generally coincide with the standard data, there are several interesting differences between the three patient groups which need discussion:

In *sex distribution* the Basel and Tel-Aviv studies showed a predominance of males over females. In the literature a 2:1 = male:female ratio is generally given (^{1, 13, 16, 18}). The New York material revealed a reverse ratio. Interestingly enough, the same ratio held true for both Whites and Negroes. The reverse ratio is possibly due to the fact that women outlive men in the United States¹⁷. Despite the small number of patients involved in the New York study the reverse ratio points out the fact that the classical inexplicable male:female = 2:1 ratio now shows less male predominance.

According to various authors (^{1, 16, 17, 18}) hypernephroma is characterized by a triad of symptoms. This „*classical triad*” which consists of: hematuria, costovertebral angle pain, and palpable tumor, does not seem to occur very often. *Soloway*¹⁹ found it in only 20 % of his cases. In our New York patient group only 7 % had a complete triad at the time of the diagnosis. If we review the symptoms separately, the following picture emerges: hematuria, in our opinion the most reliable early symptom, was found in 60–75 % of the cases in all three studies; whereas early pain appeared in 23–64 % of all our patients, constituting the second most important symptom. Thus pain appears to be more important than is generally accepted. A palpable tumor was found rather seldom (0,4 %–7 %), while fever values ranged from 1,6 %–10 %. *Voute*²² offered a new diagnostic triad: *hematuria, protracted fever and elevated sedimentation rate*. It seems justified from our point of view to add *costovertebral angle pain*. The resulting *quartet* will probably be more beneficial to the early diagnosis of hypernephroma than the classical triad.

Pyelography proved to be the diagnostic method of choice for ascertaining the diagnosis. In light of the three studies it would seem that when pyelography failed to ascertain the tumor, nephroangiography should be employed. Retroperitoneal air insufflation is no longer considered the best supplementary radiological method.

The objective of the *operation* is to gain as wide exposure as possible in order to be able to remove the kidney together with the surrounding potentially infiltrated perirenal tissue. There is no doubt that in big tumors the thoraco-abdominal method offers better access than the standard lumbar approach. Yet, the lumbar operation is still predominately used due to the fact that the thoraco-abdominal access entails a more extensive operative procedure and there is more immediate adverse effects on the often already-ill patients. We propose that in every hypernephroma patient, preoperative lung function tests should be made in order to see if the thoracic way is feasible, if deemed necessary.

The fact that the *prognosis* was best in Basel deserves discussion of some of the possible reasons:

Firstly, the Tel-Aviv cases have an interesting age distribution: in 31 % of the patients the disease occurred before the age of 51 compared with 23 % in New York and 17 % in Basel in the same age group. It is a well known fact that the younger the patient the more malignant the tumor.

Another important factor seems to be the time from the appearance of the first symptom to the time of operation. In Basel 78,5 % of the cases were operated within half a year of the first symptom, compared with only 44 % in the New York study and 52 % in the Tel-Aviv group.

In the New York study 30 % of the cases were originally, erroneously diagnosed. A neoplasma was either ascribed to some other organ or other renal disease such as nephrolithiasis were suspected. The erroneous diagnosis percentage in the Tel-Aviv survey was 36 % while in the Basel group the figure was only 9,5 %.

Hypernephroma is prone to grow into kidney veins, 65 % had tumor thrombosis on operation or at autopsy in the New York group, while Tel-Aviv had a figure of 78,5 % and Basel only 53 %.

Finally the therapy has to be considered in its influence upon the prognosis. Inoperable cases, either because of distant metastasis or a large, locally, infiltrating tumor, were found in 26 % in the New York study, in 36 % in the Tel-Aviv group and in 0,9 % in the Basel survey.

Nephrectomy combined with radiation showed a better prognosis in Basel and Tel-Aviv than in the New York series. This may be explained by the fact that the New York patients usually received radiation only when they were in an almost inoperable condition.

Summary

In order to contrast different clinical aspects of hypernephroma disease, three groups of patients, totaling 113, from three continents, all treated during the period of 1958–1963 were examined:

In spite of the fact that the "classical triad of hypernephroma" which consists of: hematuria, costovertebral angle pain and palpable tumor, has been accepted as a diagnostic standard, this study shows that a quartet of symptoms consisting of: hematuria, protracted fever, elevated sedimentation rate and costovertebral angle pain, will probably be more beneficial to the early diagnosis of hypernephroma.

The behavior of the tumor and tumor symptomatology were not found to be significantly different in the three studies.

The prognostic differences are possibly explained partly by the individual reaction of the patient to his symptoms and partly due to different standards of diagnosis and treatment in the three studies.

Bibliography

1. *Baily, H. and Love, M.*: A short practice of Surgery. Lewis & Co. London (1962).
2. *Balogh, F. and Szendrői, Z.*: Pathologie und Klinik der Nierengeschwülste. Ungarische Akademie der Wissenschaften. Budapest (1960).
3. *Beckmann, W.*: Die Ergebnisse chirurgischer Behandlung von malignen Nierentumoren. Diss. Würzburg (1958).
4. *Beer, P.*: Bösartige Nierengeschwülste, zusammenstellung von 28 Fällen aus den Jahren 1950–1958. Verlag Hallwag AG, Bern. Diss. Basel (1959).
5. *Berger, L., Marvin, W. and Sinkoff, L.*: Systemic manifestations of hypernephroma. *Amer. J. Med.* 22: 791–796 (1957).
6. *Böttiger, L. E.*: Fever of unknown origin. *Acta. Med. Scand.* 147: 133–148 (1953).
7. *Böttiger, L. E.*: Fever of unknown origin. *Acta. Med. Scand.* 156: 469–477 (1957).
8. *Dodson, A. J.*: Urologic surgery. Mosby Co., St. Louis (1956).
9. *Griffith, H. and Thackary, C.*: Parenchymal carcinoma of the Kidney. *Brit. Med. J.* 21: 128–151 (1949).
10. *Hegglin, R.*: Differentialdiagnose innerer Krankheiten. Thieme-Verlag, 9. Auflage. Stuttgart (1963).
11. *Lauffer, M.*: Vergleichende Untersuchungen an drei geographisch verschiedenen Gruppen von insgesamt 113 Fällen von Grawitzschen Tumoren aus den Jahren 1958–1963. Diss. Basel. (1965)
12. *Lenkei, S.*: Über 42 Fälle von sog. hypernephroiden, malignen Tumoren der Nieren. Aus den Jahren 1930–1950. Verlag B. Schwabe & Co., Basel. Diss. Zürich (1959).
13. *Litos, M. und Hanschke, J.*: Symptomatische Hinweise auf maligne Nierengeschwülste bei Erwachsenen. *Chir. Praxis.* 8: 419–424 (1964).
14. *Lilijestrand, A.*: Persistently high Erythrocyte sedimentation rate. *Acta. Med. Scand.* 151: 425–439 (1955).
15. *Ljunggren, E.*: Studien über Klinik und Prognose der Grawitzschen Nierentumoren. Norstedt, Stockholm (1930).
16. *Minder, J.*: Lehrbuch der Urologie. Verlag Huber, Bern (1953).
17. *Peery, T. and Miller, F. N.*: Pathology. Little & Brown, Boston (1961).
18. *Robbins, S. L.*: Textbook of Pathology. Saunders, Philadelphia (1960).
19. *Solloway, H. M.*: Renal tumors: Review of 130 cases. *J. Urol.* 40: 477–490 (1938).
20. *Thiel, T. G.*: Polycythämie bei Nierengeschwülsten. Diss. Zürich (1962).
21. *Videback, A.*: Polycythämia vera: course and prognosis. *Acta. Med. Scand.* 138: 197–187 (1950).
22. *Videback, A.*: Polycythämia vera coexisting with malignant tumors (particularly hypernephroma). *Acta. Med. Scand.* 138: 239–243 (1950).
23. *Voute, C.*: Die diagnostische Früherfassung des Hypernephromas, unter besonderer Berücksichtigung des protrahierten status febrilis. Diss. Basel (1959).

